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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/587,045

07/24/2006

Ayako Hashimoto

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8787

22852

7590

08/17/2010

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EXAMINER

CHANG, CELIA C

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/587,045	<b>Applicant(s)</b> HASHIMOTO ET AL.	
	<b>Examiner</b> Celia Chang	<b>Art Unit</b> 1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on 01 July 2010.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)    | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7/1/10</u> .  | 6) <input type="checkbox"/> Other: _____                          |

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### DETAILED ACTION

1. Amendment and response filed by applicants dated Jun. 4, 2010 have been entered and considered carefully.

Claims 1-4 as currently amended are prosecuted with compound of claim 2 and myocardial infarction as the elected species.

2. The rejection of claims 3-4 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating insufficient development and regeneration of blood vessel and various diseases cause by ischemia, does not reasonably provide enablement for *preventing* insufficient development and regeneration of blood vessel and various diseases cause by ischemia is maintained for reason of record. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to operate the invention commensurate in scope with these claims.

It was clearly delineated in the previous office action that it is unclear what is the scope of the claims under “insufficient development and regeneration of blood vessel and various diseases cause by ischemia”. Please note that insufficient development and regeneration of blood vessel can be treated with angiogenic compounds but disorder of ischemia such as myocardial infarct is irreversible cell death resulted from ischemia which is not treatable by angiogenesis.

3. The rejection of claims 1-4 under 35 U.S.C. 103(a) as being unpatentable over Fujioka et al. US 5,656,642 (cited on 1449) in view of Orito et al. Azevedo et al. and Zhou et al. is supplemented with Sumi et al is maintained for reason of record.

It was delineated in the previous office action that:

Determination of the scope and content of the prior art (MPEP §2141.01)

Fujioka et al. '642 disclosed the claimed compound being used for treating disorders that requires vasodilating. Specifically, compounds embraced by the instant claims are found in the generic formula (I) and guided by the explicit examples found in table 10 at col. 105, example 46, 52; col. 107, example 57; col. 108, example 60; col. 131 example 142; col. 143-145, examples 183, 186, 187; col. 147, example 193; col. 164-165, examples 254, 257 etc. together with activity in table 12.

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Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the instant claims and the prior art is that the utility of the disclosed compounds is for vasodilation and not enhancing angiogenesis. It is well recognized in the art that both the Fujioka et al. '642 compound (example 193 OPC-28326) and other vasodilator such as prazosin function analogously on the blood vessel (see Orito et al. p.607-610). Vasodilators such as prazosin not only caused vasodilation but also simultaneously affect the tissue to induce angiogenesis (see Azevedo et al. or Zhou et al. whole references).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in possession of the above references would be motivated to employ the Fujioka et al. compounds for enhancing angiogenesis because it is the innate nature of such compounds to simultaneously having the affect of inducing angiogenesis and a compound cannot be separated from its innate nature.

The Sumi et al. reference, although published after the filing date, provided factual support for the well known innate nature that the Fujioka et al. compounds function simultaneously as vasodilator and augments ischemia induced angiogenesis.

It is clearly set forth above that the basis of the rejection is that per ponderous of evidence indicated that adrenergic blocker which has vasodilating activity also result in the downstream angiogenesis (Orito, Azevedo or Zhou). The multiple examples fell within the generic scope of the compounds of claim 1 with vasodilating activity (Fujioka '642) and the evidence that the specific compound of claim 2 also operates by the adrenergic blocking mechanism (Orito) provided the teaching, suggestion and motivation that the group of generic compounds of the instant claim 1 would have the same downstream effect, thus, being administered for promoting angiogenesis.

Applicants argued that some vasodilators do not have such down stream angiogenic effect, thus, some unpredictability is observed. This is not persuasive because *at the time the invention was made* the teaching, suggestion and motivation were provided by the references. The post dated Sumi et al. provided *factual evidence* that such teaching, suggestion and motivation *indeed* is expected. To obviate an established obviousness based on prior art, factual evidence supporting unexpectancy commensurate with the scope of the claims must be provided.

4. The rejection of claims 1-4 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 5,656,642 in view of Orito et al. Azevedo et al. and Zhou et al. supplemented with Sumi et al. is maintained for reason of record.

No terminal disclaimer was filed.

5. References cited on the PTO-892 are those recited on the 1449 without copy or dates.

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**6. THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

**7.** Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang, Ph. D. whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet L. Andres, Ph. D., can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

*OACS/Chang*  
*Aug. 5, 2010*

*/Celia Chang/*  
*Primary Examiner*  
*Art Unit 1625*